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EXAMINER	
HIBBERT, CATHERINE S	

ART UNIT	PAPER NUMBER
1636	

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10/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/674,575	MORRIS ET AL.	
	Examiner	Art Unit	
	Catherine S. Hibbert	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-44 and 50-86* is/are pending in the application.

4a) Of the above claim(s) *42-44,50-60 and 62-66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *61 and 67-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/6/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 42-44 and 50-86 are pending. Claims 1-41 and 45-49 are cancelled. Claims 42-44, 50-60 and 62-66 are withdrawn. Claims 61 and 67-86 are under examination in this Office Action. Claims will be examined to the extent that they read on the elected inventions/species.

Election/Restrictions

Applicant's election with traverse of Group XII (claim 61) in the reply filed on 3 August 2007 is acknowledged. The traversal is on the ground(s) that Applicant states that "examining more than one invention would not constitute a serious burden". This is not found persuasive because the different inventions are likely to raise different non-prior art issues under 35 U.S.C. 112, first paragraph, the inventions require different fields of search, and the prior art applicable to one invention would not likely be applicable to another invention. In addition, Applicants election of the human STT3 sequences set forth in Table 106 (SEQ ID NO:1171 (genomic), 1172 (mRNA), and 1173 (protein) are acknowledged.

The requirement is still deemed proper and is therefore made FINAL.

Claims 42-44, 50-60 and 62-66 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 3 August 2007.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Objections

Claim 84 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 84 essentially repeats the claim limitation of claim 83 (from which it depends) which requires an increase of at least 50% relative to a control. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 61 and 67-82 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **THIS IS A NEW MATTER REJECTION.**

Applicants have amended claim 61 to add the recitation "a nucleotide sequence at least 95% identical to SEQ ID NO:1172 which encodes a polypeptide with oligosaccharyl transferase activity". In addition, new claims 67-69 include the acronym, STT3. The specification does not appear to support these recitations. Applicants are requested to delete the new matter or clearly establish where support is found in the specification for the claimed method comprising detecting differential expression of STT3 or a nucleotide sequence at least 95% identical to SEQ ID NO:1172 which encodes a polypeptide with oligosaccharyl transferase activity.

Claims 68-82 are rejected insofar as they depend from claims 61 and 67.

Claims 61, 67-70, 73-78, and 80-82 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claims are directed to methods of diagnosing colon cancer comprising determining the level of expression product having at least 95% sequence identity to a sequence of SEQ ID NO: 1172, and encoding a polypeptide with oligosaccharyl transferase activity or of SST3. The written description is not commensurate in scope with these method claims drawn to a method of detection of sequences having at least

95% sequence identity to a sequence of SEQ ID NO: 1172, and encoding a polypeptide with oligosaccharyl transferase activity or of SST3, which have not been adequately described nor evidenced to be in the possession of Applicants. Applicants seem to only be in possession of SEQ ID NO: 1172. "Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was 'ready for patenting' such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identify characteristics sufficient to show that the applicant was in possession of the claimed invention", see Official Gazette, 1242 OG 172, January 30, 2001.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).
Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

The skilled artisan cannot envision the detailed structure of nucleotide sequences only 95-98% identical to SEQ ID NO: 1172 (having oligosaccharyl transferase activity), as well as SST3 and conception is not achieved until reduction to practice has occurred. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The product itself is

required. Applicants have not described nucleotide sequences only 95-98% identical to SEQ ID NO: 1172 (having oligosaccharyl transferase activity), as well as SST3 with sufficient particularity such that one skilled in the art would recognize that the Applicants had possession of the claimed invention. See Fiers v. Revel, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Lts., 18 USPQ2d 1016.

Furthermore, In The Reagents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic statement, which defines a genus of nucleic acids by only their functional activity, does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

In the instant case, Applicants have provided no representative examples of the sequences which are claimed other than the SEQ ID NO: 1172.

Claims 61 and 67-86 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to

which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification does not reasonably provide enablement for a method of diagnosing colon cancer.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is required is not based upon a single factor, but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:

1) Unpredictability of the art. The art in the area of colon cancer diagnosis using any patient sample and by detecting the gene expression products associated with STT3 and/or SEQ ID NO:1172 is unpredictable. The research required to determine whether the differential gene expression of candidate gene expression products is diagnostic for colon cancer is extremely complex. It is difficult or impossible to *a priori* predict whether the differential expression (claims 61, 67, 69-74, 78-79), and more specifically up-regulation (claims 68, 75-77, 80-86) of specific genes taken from any patient sample is actually diagnostic for colon cancer. It is difficult or impossible to predict whether the differential gene expression, as claimed, of STT3 and/or SEQ ID NO:1172 is diagnostic for colon cancer because, for example, the results can be dramatically different depending on whether the colon cancer is an aggressive metastatic-type or a slow-growing low metastatic-type. Indeed, even the identification of

a nucleic acid which encodes a gene product which may indicate a diagnosis for cancer can give conflicting results depending, for example, on whether the patient sample is taken from cells nearer to the necrotic core of the tumor or nearer to the vascularized cells which are undergoing faster cell replication, and therefore is an endeavor which requires extensive inventive research. Examples of the type of research required to identify a putative cellular expression product, which is a colon cancer diagnostic, are exemplified by Kelleher et al in "Oligosaccharyltransferase isoforms that Contain Different Catalytic STT3 Subunits Have Distinct Enzymatic Properties" (Molecular Cell, Vol 12, 101-111, July, 2003) and Williams et al in "Human Genes and Gene Expression Products" (US Patent 6,964,868, filed 28 January 1999).

2) State of the art. The art with regard to methods for detecting colon cancer using STT3 and or SEQ ID NO:1172 must be considered to be experimental. Although researchers have contemplated using STT3 (also called SIMP) expression products for colon cancer detection (see Williams et al and below, Prior Art Rejection under 102 (e)), the invention, as claimed, which uses any patient sample, has not been shown in the prior art to be diagnostic for colon cancer.

3) Number of working examples. Applicants present no working examples of the claimed invention in the specification.

4) Amount of guidance provided by applicants. Applicants present no guidance on the practicing of the claimed invention with any of the claimed molecules. Applicants present no teachings on how the detection of differentially expressed STT3/SEQ ID

NO:1172 expression products using any patient sample is an effective method for diagnosing colon cancer.

5) Scope of the claims. The claimed invention is broad in scope. The invention reads on any patient sample (claims 61 and 67-86) and the patient sample, as claimed, does not read on colon tissue.

6) Nature of the invention. The invention involves complex, unpredictable, aspects of gene expression, tumor morphology, and intricate differences between oligosaccharyl transferase isoforms which have distinct enzymatic properties.

7) Level of skill in the art. The level of skill in the art is high; however, given the complex, unpredictable aspects of the invention, the lack of guidance presented by applicants, the lack of working examples and the broad scope of the invention, it must be considered that the skilled artisan would have had to have conducted undue and excessive experimentation in order to practice the claimed invention.

Given the analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be considered that the skilled artisan would have had to have practiced essentially trial and error experimentation in order to try to practice the claimed invention. Said experimentation must be considered to be undue and excessive.

Claim Rejections - 35 USC § 102/ 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 61 and 67-86 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Perreault and McBride in "Mammalian SIMP protein, gene sequence and uses thereof in cancer therapy" (US PGPUB 2003/0148285A1, filed 20 December 2001) (see Score Report 10674575, 2007/08/06 database: rapbm, Result 1: SEQ ID NO:2).

Independent claim 61 is directed to a method for diagnosing colon cancer comprising: a) determining the level of an expression product in a patient sample; said expression product comprising or encoded for by a nucleic acid comprising a sequence at least 95% identical to SEQ ID NO:1172; and b) comparing said level of the expression product in (a) to a level of the expression product in a second sample, said

second sample comprising a normal tissue; wherein a difference between the level of the expression products in (a) and the level of the expression products in the second sample indicates that the patient has colon cancer; wherein said nucleotide sequence at least 95% identical to SEQ ID NO: 1172 encodes a polypeptide with oligosaccharyl transferase activity. Further limitations are drawn to the method of claim 61 wherein the expression product is a mRNA having a sequence at least 98%/100% identical to SEQ ID NO: 1172 (claims 78/79). Further limitations are drawn to the method of claim 61 wherein the level of the expression product in the sample is increased at least 50%/100%/150% relative to the control (claims 80/81/82).

Independent claim 67 is directed to a method for diagnosing colon cancer comprising detecting evidence of differential expression of STT3 in a patient sample wherein evidence of differential expression of STT3 indicates that the patient has colon cancer. Further limitations are drawn to the method of claim 67, wherein STT3 gene expression in the patient sample is up-regulated relative to STT3 gene expression in normal tissue (claim 68), wherein evidence of differential expression is detected by measuring the level of an expression product of STT3 (claim 69), and further to wherein the expression product is a mRNA having a sequence at least 98%/100% identical to SEQ ID NO: 1172 (claim 71/72), to wherein the expression product is a polypeptide or mRNA/wherein the level of expression product in the patient sample is compared to a control (claim 70/73), and further to wherein the control is a known normal tissue of the same tissue type as in the patient sample (claim 74).

Further limitations are drawn to the method of claim 73 wherein the level of the expression product in the sample is increased at least 50%/100%/150% relative to the control (claims 75/76/77).

Independent claim 83 is directed to a method of diagnosing colon cancer comprising: a) determining the level of a nucleotide sequence that hybridizes under highly stringent conditions to SEQ ID NO:1172, or a complement thereof, in a patient sample; wherein hybridization is performed at 50°C to 60°C in 5 X SSC (9 mM saline/0.9 mM sodium citrate); and b) comparing said level of nucleotide sequence in (a) to a level of the nucleotide sequence in a second sample, said second sample comprising a negative control comprising non-cancerous tissue; wherein an increase of at least 50% between the level of the nucleotide sequence in (a) and the level of the nucleotide sequence in the second sample indicates that the patient has prostate cancer, colon cancer, stomach cancer or breast cancer. Further limitations are directed to the method of claim 83 wherein the level of the nucleotide sequence in (a) is increased at least 50%/100%/150% relative to the control (claims 84/85/86).

Perreault and McBride teach a sequence (SEQ ID NO:2) that has 99.7 % identity to the polypeptide encoded by the instant nucleic acid SEQ ID NO:1172 mRNA, which is the instant SEQ ID NO:1173 polypeptide. Perreault and McBride teach the nucleic acids which encode the polypeptide, which is called the mammalian SIMP gene sequence. The mammalian SIMP gene sequence is a synonym and/or homolog for STT3 and encodes a polypeptide with oligosaccharyl transferase activity. Furthermore, Perreault and McBride contemplate a method for diagnosing different types of cancer,

including colon cancer, by detecting differential gene expression of the product which is 99.7% identical to Applicants claimed oligosaccharyl transferase/STT3 sequences.

For example, Perreault and McBride recite:

> Determination of the amount of SIMP or fragment thereof in a biological sample may be especially useful for diagnosing a cell proliferative disease or an increased likelihood of such a disease, particularly in a human subject, using a SIMP nucleic acid probe or SIMP antibody. Preferably the disease is a rapidly growing cancer or a cancer that displays a short doubling time (e.g. hematopoietic cancer, lung cancers, prostate cancer, testis cancer, breast cancer, melanomas, pancreatic cancer intestine cancers, sarcomas, prostate cancer and hematologic cancers). This may be achieved by contacting, in vitro or in vivo, a biological sample (such as a blood sample or a tissue biopsy) from an individual suspected of harboring cancer cells, with a SIMP antibody or a probe according to the invention, in order to evaluate the amount of SIMP in the sample or the cells therein. The measured amount would be indicative of the probability of the subject of having proliferating tumoral cells since it is expected that these cells have a higher level of SIMP expression (paragraph 0178).

In addition, Perreault and McBride contemplate wherein the expression product is at least 128% relative to a control, stating that "the number of copies of B6.sup.dom1 MiHA per cell (a peptide from mSIMP) was shown to increase by 128-fold on mitogen activated T-cells relative to resting splenocytes" (paragraph 0124, lines 4-5).

Furthermore, Perreault and McBride contemplate detection of the SIMP/STT3 expression products using highly stringent hybridization conditions (see especially paragraph 0147).

The claim limitations recited in claims 77,82, and 86 with regards to the increased expression levels of "at least 150%" compared to the control levels is not explicitly described in the Perreault and McBride reference. However, the Perreault and McBride reference cite increased expression levels of at least 128%. It would be inherent in the method of Perrault and McBride to detect levels above the 128% levels, including levels of at least 150% above the control levels.

Therefore, Perreault and McBride anticipate/render obvious the instant claims 61, 67-86.

It is noted that this Office Action contains rejections of the same claims under 35 USC 112, 1st (enablement) and 35 USC 102(e)/(a) and 103(a). While these rejections may seem contradictory, they are not because each is based upon a different legal analysis, i.e. sufficiency of the disclosure of the instant application to support claims under 35 USC 112, 1st paragraph vs. sufficiency of a prior art disclosure to anticipate or render obvious an embodiment(s) of the claimed invention (See *In re Hafner*, 161 USPQ 783 (CCPA 1969)).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Catherine S. Hibbert whose telephone number is 571-270-3053. The examiner can normally be reached on Monday-Friday, 7:30 AM-5:00 PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Respectfully submitted,

Catherine S. Hibbert/AU1636

DAVID GUZO
PRIMARY EXAMINER